of this sequence search and to discuss the cited art and its relationship to the claimed invention, applicant specifically requests an Examiner's Interview. Applicant will attempt to contact the Examiner approximately one month after the filing of this paper to arrange a convenient date. The Examiner may contact the applicant at the number provided on the final page of this paper.

Comments on the Specification and Drawings

Applicant will address the arrangement of the specification and the formality of the drawings upon indication of allowability.

Rejection under 35 U.S.C. § 112, second paragraph

The PTO rejects claims 1-7 as indefinite.

Applicant has amended claim 1 to remove the word "discriminating," which the PTO objected to.

The PTO questions the use of the word "subsequences" in claims 1-5. Applicant points out that this word is used throughout the specification. One skilled in the art can determine the meaning of "subsequences" from the specification.

Applicant has amended claim 1 to correct the antecedent basis for the "oligonucleotide probes."

Applicant has amended claim 1 to address the "hybridization reactivity" of operon subsequences.

Applicant has amended claim 1 to remove the word "relative."

Applicant has amended the preamble to claim 1.

Applicant has amended the recitation of "probe SEQ ID NO." in claims 2-7.

Applicant has amended claim 6 to recite a proper Markush format.

This rejection has been overcome or is in error. Applicant requests the PTO withdraw it.

Rejection Under 35 U.S.C. § 102(b)

Applicant has canceled claim 7, without prejudice. New claim 8 has been added.

Applicant has reviewed the Cilia document and nowhere finds a sequence that contains any of Sequences 1-4 of the claims, as asserted in the Office Action. In fact, it appears that only a maximum of 9 bases of only one sequence is discussed. As noted above, applicant does not have a

copy of the sequence search results mentioned in the Office Action. Whatever those results are, if they are based on Cilia, they do not appear to properly disclose the sequences claimed.

In addition, applicant's new claim 8 recites probes that are capable of distinguishing between species. None of these aspects are mentioned in the cited art.

Applicant requests the withdrawal of this rejection.

Rejection Under 35 U.S.C. § 103(a)

Claim 1 stands rejected as the PTO considers it unpatentable over Kohne (U.S. Patent 5,601,984). Claims 2-6 stand rejected as the PTO considers them unpatentable over Kohne in view of Cilia. Applicant respectfully disagrees.

Initially, applicant points out that prior to this invention, no method or sequences were capable of distinguishing between certain species of bacteria, especially the Shigella and E. coli species detailed in the specification. As discussed at pages 5 and 6 of the specification, the presence of subsequence variations within an operon, even within the same species of a single organism, can confound hybridization attempts to detect individual species within a sample.

Kohne never addresses the type of manipulation that can allow a hybridization assay to distinguish between closely related species, or strains within a single species. Kohne merely refers to the ability to distinguish between species because of a "lack of conservation" (col. 6, lines 9-12). However, applicant's method can distinguish even where a lack of conservation does not exist. In addition, Kohne never addresses the use of operons as elements of a hybridization analysis. Furthermore, Kohne never addresses the selection and determination of subsequences from an operon that can successfully distinguish closely related species. Therefore, whatever types of hybridization Kohne discusses, they do not teach or suggest a method as applicant has claimed. Furthermore, the only data Kohne provides employs the enzyme reverse transcriptase to fashion c-DNA probes. Reverse transcriptase is known to have a very high error rate for transcribing RNA into c-DNA, which would further obscure detection of small differences between intra- and interspecies base sequences. Kohne's method in Example 2 (Table 6) fails to distinguish between 11 different species of *Legionella.*

Cilia does not discuss hybridization assays but merely compares sequences of E. coli operons. Whatever Cilia adds to a combination of teachings with Kohne, it does not provide a

specific teaching to use subsequences of an operon to make a hybridization assay. There is simply no objective motivation to arrive at a method as applicant claims.

Applicant requests the withdrawal of this rejection.

Conclusion

All of the stated grounds of objection and rejection have been traversed or rendered moot. Applicant believes that this constitutes a full and complete response to the outstanding Office Action and that the application is now in condition for allowance. If the Examiner believes, for any reason, that a personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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Attachment:
ABSTRACT, one sheet

Date: 2-7-2000